Research Journal of Medicinal Plant

ISSN 1819-3455

Academic Journals Inc.

www.academicjournals.com

Research Journal of Medicinal Plant 1 (4): 134-138, 2007
ISSN 1819-3455

Antidiabetic Effects of *Homalium letestui* (Flacourtiaceae) in Streptozotocin Induced Diabetic Rats

[1]Jude E. Okokon, [2]Bassey S. Antia and [2]Basil N. Ita
[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy,
[2]Department of Chemistry, University of Uyo, Uyo, Nigeria

Abstract: Evaluation of antidiabetic activity of ethanolic root extract of *Homalium letestui* in rats was carried out. Antidiabetic potentials of the plant *Homalium letestui* extract (500-1000 mg kg^{-1}) was investigated in streptozotocin induced diabetes in rats. Treatment of streptozotocin diabetic rats with the extract caused a significant ($p<0.01$) reduction in fasting Blood Glucose Levels (BGL) of the diabetic rats both in acute study and prolonged treatment (2 weeks). The activity of the extract was comparable to that of the reference drug, glibenclamide. This results suggest that the root extract of *Homalium letestui* possesses antidiabetic effect on streptozotocin induced diabetic rat.

Key words: Antidiabetic, streptozotocin, *Homalium letestui*, hypoglycaemia, blood glucose

INTRODUCTION

Diabetes is one of the oldest known diseases of man whose devastating effect is increasing by the day and severity almost at epidemic level. Diabetes is a disease of disordered metabolism of carbohydrate, protein and fat which is caused by the complete or relative insufficiency of insulin secretion and/or insulin action (Balkau *et al*., 2000). The number of people suffering from the disease worldwide is increasing at an alarming rate with projected 366 million people likely to be diabetic by the year 2030 against 191 million estimated in 2000 (Wild *et al*., 2004).

Among the major factors, besides hyperglycemia, which complicate diabetic state and result in death is hyperlipidaemia (Nabel, 2003; Nagappa *et al*., 2003). Developing countries are the most affected because of expensive and inadequate treatments (Djrolo *et al*., 1998), coupled with the side effects associated with these drugs, thus the search for a new drug with low cost, more potentials and without adverse effects become inevitable. A great number of medicinal plants have been used in the treatment of diabetes in different parts of the world, some of which are without scientific scrutiny although World Health Organisation (WHO) had encouraged and recommended the use of plants as an alternative therapy for diabetes (WHO, 1980). Evaluation of the antidiabetic potentials of these plants becomes necessary to provide scientific proof and justify their use in ethnomedicine.

Homalium letestui Pellegr (Flacourtiaceae) is a forest tree growing up to 80-100 feet and found in the rainforest of West Africa (Hutchinson and Daziel, 1963; Keay, 1989). The plant parts particularly the stem bark and root are used in various decoctions traditionally by the Ibibios of Niger Delta of Nigeria to treat stomach ulcer and malaria as well as an aphrodisiac. Okokon *et al*. (2006) reported of the antimalarial activity of the plants with LD50 of 4.47 g kg^{-1}. Report of scientific studies on *Homalium letestui* are few and there is no information regarding the hypoglycaemic activity of *H. letestui* root extract in rats. The present study, therefore, was designed to establish if the roots of *H. letestui* has any antidiabetic effects on STZ induced diabetic rats.

Corresponding Author: Jude E. Okokon, Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo, Uyo, Nigeria Tel: +234802-345-3678

MATERIALS AND METHODS

Plant Materials

The roots of *Homalium letestui* were collected from a forest in Ikono area of Akwa Ibom State of Nigeria and authenticated by Dr. Margaret Bassey, a Taxonomist in the Department of Botany, University of Uyo, Uyo, Nigeria. A voucher specimen was deposited in the Faculty of Pharmacy Herbarium, University of Uyo, Uyo (Voucher No. FPUU 382). The plant material were dried at room temperature and then powdered using laboratory mortar.

Preparation of Extract

The dried and powdered roots of *H. letestui* (1 kg) was exhaustively macerated in 70% ethanol for 72 h. The liquid extract obtained was concentrated in vacuum at 40°C. The yield was 2.88%.

Animals

Albino wistar rats (105-165 g) of either sex were obtained from the University of Uyo animal house. They were maintained on standard animal pellets and water *ad libitum*. The study was conducted in Pharmacology and Toxicology Department, Faculty of Pharmacy, University of Uyo, Uyo, Ngeria in August 2006. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo.

Chemicals and Drugs

Streptozotocin was purchased from sigma chemical Co, St. Louis, MO, USA, Glibenclamide (Daonil) was gotten from Aventis, Germany. All the other chemicals used were of analytical grade.

Induction of Diabetes

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared solution of Streptozotocin (55 mg kg^{-1} body weight) in ice cold 0.9% NaCl saline solution. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemia. Control rats were injected with normal saline alone. One week was allowed for the development of diabetes, rats with moderate diabetes having glycosuria and hyperglycemia (blood glucose level range above 200 mg dL^{-1}) were considered as diabetic and used for the drug treatment. The root extract in aqueous solution was administered orally through a gavage at a concentration of 200 mg kg^{-1} body weight $rats^{-1}$ day^{-1} for 14 days.

Experimental Design

The animals were divided into 5 groups of 6 animals each for the evaluation of antidiabetic activity.

Group I: Diabetic rats administered *Homalium letestui* extract (500 mg^{-1} kg^{-1} rat^{-1} day^{-1}) in acqueous solution orally for 14 days.

Group II: Diabetic rats given *H. letestui* extract (750 mg^{-1} kg^{-1} rat^{-1} day^{-1}) in aqueous solution orally for 14 days.

Group III: Diabetic rats administered *H. letestui* extract (1000 mg^{-1} kg^{-1} rat^{-1} day^{-1}) in aqueous solution.

Group IV: Diabetic rats given Glibenclamide (10 mg^{-1} kg^{-1} rat^{-1} day^{-1}) for 14 days in aqueous solution orally for 14 days.

Group V: Diabetic control rats.

The body weight gain and fasting Blood Glucose Levels (BGL) of all the rats were recorded at regular intervals during the experimental period. For acute study, the BGL was monitored after 1, 3, 5 and 7 h of administration of a single dose of the extract and at the end of 1, 3, 5, 7 and 14 days for prolonged treatments. The BGL was monitored in the blood of the diabetic rats by tail tipping method. The blood was dropped on the dextrostix reagent pad. This was inserted into microprocessor digital blood glucometer and the readings were noted (WHO, 1980).

Statistical Analysis

All the group data were statistically analysed with Students' t-test and two-way ANOVA, followed by Tukey Krammer post test. Values of $p<0.05$ were considered significant.

RESULTS AND DISCUSSION

There were observable changes in body weight of treated and untreated rats. Significant weight loss was observed in the untreated diabetic rats. Treatment of diabetic rats with ethanolic root extract of *H. letestui* or Glibenclamide improved the weight gain compared to untreated diabetic rats (Table 1). Dose dependent reduction in BGL was observed in STZ induced diabetic rats treated with ethanolic root extract of *H. letestui*. After a single dose of the extract on the streptozotocin diabetic rats, there was a significant ($p<0.05$) reduction in BGL of the diabetic rats within the period of acute study which was seven hours compared to the control. The effect was more significant than that of the standard drug, Glibenclamide (Table 2). During prolonged study (14 days), the extract produced a sustained significant ($p<0.01$) reduction in BGL of the diabetic rats compared to control (Table 3).

Table 1: Effect of treatment with ethanolic root extract of *H. letestui* on body weight of streptozotocin induced diabetic rats

		Average body weight (g)	
Drugs	Dose (mg kg^{-1})	Day 0	Day 15
Control	0	239.5±3.10	203.9±2.60
Extract	200	229.0±0.10*	264.3±4.30*
	400	216.0±24.5*	233.0±9.20*
	600	237.5±9.50*	371.0±11.5*
Glibenclamide	10	256.0±2.20*	286.0±8.70*

Values are expressed as mean+SEM, *: $p<0.05$ (n = 6) (Students' t-test)

Table 2: Effect of *Homalium letestui* on blood glucose levels of streptozotocin diabetic rats after a single dose

		Blood glucose level (mg dL^{-1}) (Mean±SD)					
Drugs	Dose (mg kg^{-1})	Initial	1 h	3 h	5 h	7 h	24 h
Control	0	231.6±15.5	240.3±2.70	245.6±1.30	258.2±2.10	264.3±1.90	266.0±1.63
Extract	1000	225.5±8.51	229.0±5.00*	156.1±3.80*	135.0±1.00*	112.0±19.0*	40.5±0.50
	750	274.5±9.50	192.0±6.00*	169.0±5.00*	140.0±2.00*	112.0±2.40*	47.0±2.64
	500	200.8±12.8	235.5±9.50*	192.0±5.00*	142.0±9.50*	93.5±9.50*	50.5±15.5
Glibenclamide	10	247.2±5.50	193.5±1.80*	156.1±3.80*	130.3±4.10*	93.2±6.80*	78.2±2.80

*: $p<0.01$ when compared to control, F-11.75, 12.08, df = 4,16 ($p<0.01$), two-way ANOVA), n = 6 per group

Table 3: Effect of *Homalium letestui* on blood glucose levels of streptozotocin diabetic rats during prolonged treatment

		Blood glucose level (mg dL^{-1}) (Mean±SD)				
Drugs	Dose (mg kg^{-1})	Initial	3rd day	5th day	7th day	14th day
Control	0	231.6±15.5	271.64±9.10	275.3±3.40*	280.2±2.70	282.3±9.10
Extract	500	225.5±8.51	208.50±0.50*	151.5±13.50*	105.0±3.50*	92.0±2.50*
	750	274.5±9.50	192.00±8.50*	65.5±5.50*	84.0±10.3*	86.0±5.10*
	1000	200.5±9.50	124.00±4.30*	64.5±0.50*	70.6±5.50*	65.0±7.80*
Glibenclamide	10	247.2±5.50	73.80±3.20*	69.5±0.50*	67.6±3.80*	65.1±8.20*

*: $p<0.01$ when compared to control, F = 9.20, 11.16, df = 20,5 ($p<0.01$) (Two-way ANOVA) n = 6 per group

Evaluation of antidiabetic activity using streptozotocin induced hyperglycaemia model has been described by Szkudelski (2001) to be very useful. Streptozotocin selectively destroys the pancreatic insulin secreting beta cells, leaving the less active cells thus resulting in a diabetic state (Kamtchoung *et al*., 1998; Szkudelski, 2001) Glibenclamide is often used as a standard drug to compare the efficacy of the hypoglycaemic agents in STZ-induced diabetes. In this study, acute and prolonged treatment of STZ-induced diabetic rats with various doses of the *H. letestui* extract produced a significant ($p<0.05$) reduction in BGL of the rats in a manner comparable to that of the standard drug. The treatment also caused a significant increase in weight of the animals which is attributable to the extracts' hypoglycaemic activity. This hypoglycaemic effect of the extract is linked to the presence of flavonoids and terpenes in the extract (Okokon *et al*., 2006). These compounds have been implicated in the antidiabetic activities of many plants (Shimizu *et al*., 1984; Reher *et al*., 1991; Ivorra *et al*., 1989). The hypoglycaemic action of this extract may be by potentiating the insulin effect, either by increasing the pancreatic secretion of insulin from the cells of islets of langerhans or its release from bound insulin (Pari and Armanath, 2004).

In conclusion, the present study shows that the ethanolic stembark extract of *H. letestui* has potential hypoglycaemic action on STZ-induced diabetic rats and the effect was found to be comparable to glibenclamide. Further studies to isolate and identify the active principle as well as elucidation of its mode of action is necessary.

ACKNOWLEDGMENT

The authors are grateful to Mr. Nsikan Malachy of Pharmacology and Toxicology Department, University of Uyo, Uyo, for his technical assistance.

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